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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/856,676

07/16/2001

Zheng Xin Dong

00537-187002

2104

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01/30/2007

EXAMINER

BORIN, MICHAEL L

ART UNIT

PAPER NUMBER

1631

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

01/30/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

# Office Action Summary

Application No.

09/856,676

Applicant(s)

DONG ET AL.

Examiner

Michael Borin

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 26 October 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-9 is/are pending in the application.  
4a) Of the above claim(s) 6 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5, 8 and 9 is/are rejected.
- 7) ☒ Claim(s) 7 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Status of the application***

Applicant filed RCE request concurrently with arguments about the finality of the preceding Office action. The RCE request was processed before forwarding the application to the Examiner. Applicant's argument that finality of the previous Office action was premature is deemed convincing. However, at the time Examiner considered the response the application would have been past 6-month statutory period to respond and become abandoned, had Request for Continuing Consideration had not been previously entered. No Notice of Appeal or response after-final had been submitted. Therefore, to maintain pendency of the application, the RCE status of the application is maintained.

### ***Claim Rejections - 35 USC § 103***

Claims 1-5, 8, 9 are rejected under 35 U.S.C. 103(a) as obvious over Buckley et al. (US Patent 5,545,618) and Galloway et al. (EP 733644 A1).

Claim 8 recites the following related derivatives of hGLP-1(7-36)-NH<sub>2</sub>:



Buckley and Galloway teach biologically-active hGLP-1 analogs and their pharmaceutical compositions. Buckley teaches that truncation of GLP-1 to 7-34, 7-35,

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7-36 or 7-37 fragments does not alter its biological activity. Ala<sup>8</sup> is the residue in position 8 in natural GLP-1 (see col. 2, bottom). This Ala residue can be replaced with an alternative small neutral amino acid residue, such as Gly (see col.3, line 25, and Fig.1). Also, the residue in 8-th position may be either in L- or D-configuration (see col. 3, lines 35-37). Galloway teaches that Ala or Gly, as well as  $\alpha$ -methyl Ala<sup>8</sup> are preferred residues in 8-th position. See p. 4, lines 37-54.

The references do not teach N-Me derivatives of Ala<sup>8</sup>-hGLP-1(7-36)-NH<sub>2</sub>, Ala<sup>8</sup>-hGLP-1(7-36)-NH<sub>2</sub>, or Gly<sup>8</sup>-hGLP-1(7-36)-NH<sub>2</sub>, as instantly claimed. Within the context of chemistry, unsubstituted compounds are similar to their homologue, lower alkyl (e.g., methyl) substituted compounds in the physical properties, and, because of their structural similarity, it is generally predictive that their chemical properties will be similar. Because the adjacent homologs, lower alkyl compounds - N(lower alkyl)-, would be expected to have similar physical and chemical properties as unsubstituted (-NH-) compounds, a high degree of predictability in producing a compound having the same physical and chemical properties would be expected when substituting H for lower alkyl group in a large compound. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the preferred Ala<sup>8</sup> or Gly<sup>8</sup> GLP-1 analogs of Buckley or Galloway such that NH- group is replaced by N-Me group. Since one of ordinary skill in the art of pharmaceutical chemistry would have expected that such modification would not change the properties of a compound in a significant way, one of ordinary skill in the art would have been motivated to make such

a modification so as to obtain another preferred compound with the activity disclosed in Buckley and Galloway.

Response to arguments

Applicant argues that Buckley teaches away from preparing N-alkylated derivatives because the reference teach that such derivatives have enhanced degradation resistance. Applicant considers such property as "different biological property". Examiner respectfully disagrees. Enhanced degradation resistance not a "different biological property"; rather, it is an additional beneficial property which is a desirable pharmaceutical effect pursued by the referenced method.

The same applies to a citation from unidentified "one of the references" which addresses N-methyl derivatives of leuprolide as being more stable.

With respect to the Declaration of Dr. Dong filed 10/26/2006, the Declaration is insufficient to overcome the rejection for the following reasons. The Declaration acknowledges "that structural similarity is generally predictive of similar physical and chemical properties". Therefore, one would expect that replacing NH- group with N-Me group will not change the existing properties of the referenced compounds. Second, the argument in the Declaration that modifying compounds by preparing N-Me homologs would "protect peptide bonds against enzymatic cleavage", i.e., improve their stability, is not an unexpected beneficial property, as the Buckley teaches exact same effect of N-alkylation – enhanced degradation resistance (col. 3, lines 45-64, as discussed by applicant in the response). compounds aproperties of a compound in a significant way, one of ordinary skill in the

**Conclusion.**

No claims are allowed.

Claim 7 is novel and unobvious over the prior art of record or any combination thereof. The prior art of record does not teach or suggest hGLP-1(7-36)-NH<sub>2</sub> derivatives claimed in claim 7.

Claim 7 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

This is an RCE of applicant's Application No.09/856676. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Michael Borin, Ph.D.  
Primary Examiner  
Art Unit 1631

mlb